REMARKS

This amendment is being resubmitted to correct status identifiers and typographical errors. No new matter has been added.

Claim 51 is withdrawn, and has now been incorporated in claim 52. Claims 59, 64, 68, 69, 70, 71, and 72 have been amended to correct dependency. Claims 53, 54, 55, 66, and 67 have been amended for clarification. Claims 52, 53, 55, 57, 58, 65, and 67 are currently active in the application.

The present invention provides a composition, for delivery of a therapeutic agent to a neuronal cell, comprising the therapeutic agent, a neuronal cell targeting component, and a translocation domain (page 3, line 36 to page 5, line 7 of the present application). In the claims as amended, the therapeutic agent is an ADP-ribosyltransferase. Without being bound to any particular theory, it appears that ADP-ribosyltransferases act by ADP-ribosylation of Rho GTPases (page 8, lines 25-30).

The rejection of the claims as being anticipated by Shone *et al.* (WO 00/28041) is respectfully traversed. The cited reference fails to disclose or suggest a composition comprising a therapeutic agent wherein the therapeutic agent is an ADP-ribosyltransferase.

Shone *et al.* describes a composition for the delivery of superoxide dismutase to neuronal cells. The composition includes a superoxide dismutase (SOD) linked to a neuronal targeting component, which component includes a first domain that binds to a neuronal cell and a second domain that translocates the SOD into the neuronal cell (Abstract). The linker is cleavable and thus, in use, after translocation of the SOD into the cell, the linker is cleaved to release SOD from the neuronal cell targeting domain (page 5, last paragraph).

In the rejection, reference is made to Heo *et al.* (J. Biol. Chem., 280: 31003-31010, 2003) to show that SOD abolishes Rac1 guanine nucleotide dissociation, therefore allegedly inhibiting a Rho GTPase.

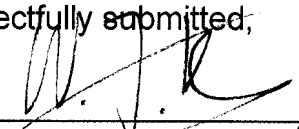
As noted above, the claims as amended are drawn to a composition comprising an ADP-ribosyltransferase. SOD is not an ADP-ribosyltransferase. Rather, SOD catalyzes the dismutation of superoxide ion into molecular oxygen and hydrogen

peroxide ($O_2^- \rightarrow O_2 + H_2O_2$). Accordingly, SOD and ADP-ribosyltransferase are different enzymes, catalyzing different reactions. Accordingly, all the elements of the claims as amended are not present in Shone *et al.*

Furthermore, nowhere does Shone *et al.* describe or suggest a composition comprising an ADP-ribosyltransferase, a neuronal cell targeting component, and a translocation domain. Unless a composition is tested, there is no way of predicting its activity on neuronal cells and therapeutic potential. The delivery of ADP-ribosyltransferase to neuronal cells achieved by the present invention is thus unpredictable in view of the cited reference. The present invention is therefore neither anticipated by nor obvious over the cited reference. Withdrawal of this ground of rejection is respectfully requested.

Applicants submit that the present application is now in condition for allowance. Early notice of such action is respectfully requested.

Respectfully submitted,



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